

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No. 38005-0183

In re patent application of:
Martin OPPER et al.

Confirmation No.

Serial No.: Unassigned

Art Unit: Unassigned

Filed: August 4, 2003

Examiner: Unassigned

For: CYTOPLASMIC EXPRESSION OF ANTIBODIES, ANTIBODY FRAGMENTS
AND ANTIBODY FRAGMENT FUSION MOLECULES IN E. COLI

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56 and 37 CFR §1.97

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Submitted herewith on Form PTO/SB/08A is a listing of documents known to applicants in order to comply with applicants' duty of disclosure pursuant to 37 C.F.R. §1.56.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or is considered to be material to patentability as defined in 37 C.F.R. §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* prior art reference against the claims of the present application.

The documents submitted herewith on Form PTO/SB/08A, lists the documents cited by or submitted to the Patent Office in parent application Serial No. 09/273,453 filed March 22, 1999 (now U.S. Patent No. 6,602,688), which is a Divisional of U.S. Serial No. 08/630,820 filed April 10, 1996 (now U.S. Patent No. 6,008,023).

As provided in 37 C.F.R. §1.98(d), copies of the documents are not being provided since they were previously cited by or submitted to the Patent Office in parent application Serial No. 09/273,453 filed March 22, 1999 (now U.S. Patent No. 6,602,688), which is a Divisional of U.S. Serial No. 08/630,820 filed April 10, 1996 (now U.S. Patent No. 6,008,023).

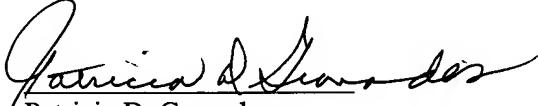
The instant Information Disclosure Statement is being filed in compliance with 37 CFR §1.97(b) within three months from the filing date of the above-identified application, therefore, no fee is required in connection with its filing. However, the Commissioner is hereby authorized to charge any deficiency or to credit any overpayment to Deposit Account No. 08-1641.

Applicants respectfully request that the listed documents be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO-SB/08A be returned in accordance with M.P.E.P. §609.

Respectfully submitted,

August 4, 2003

Date


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INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>		Application Number	Unassigned
		Filing Date	August 4, 2003
		First Named Inventor	Martin OPPER et al.
		Group Art Unit	Unassigned
		Examiner Name	Unassigned
		Attorney Docket Number	38005-0183
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FOREIGN PATENT DOCUMENTS							
Examiner Initials*	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Office ³	Number ⁴	Kind Code ⁵ (if known)			
	A02	EP	0 501 215			9/92	
	A03	EP	0 623 352			4/94	
	A04	EP	0590530	A	SEEMAN et al.	2/10/1992	
	A05	EP	0590530	A2	GEHRMANN et al.	9/24/93	

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¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

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		Attorney Docket Number	38005-0183

OTHER PRIOR ART -- NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
	A06	GUSSOW et al.; "Humanization of Monoclonal Antibodies", Methods in Enzymology; Vol. 203; (1991); pp. 99-121	
	A07	BOSSLER et al.; "Molecule and Functional Characterization of a Fusion Protein Suited for Tumor Specific Prodrug Activation"; Br. J. Cancer; Vol. 65; (1992); pp. 234-238	
	A08	DERMAN et al.; "Mutations that Allow Disulfide Bond Formation in the Cytoplasm of Escherichia Coli"; Science; Vol. 262; (1993); pp. 1744-1747	
	A09	JEFFERSON et al.; "B-Glucuronidase from Escherichia Coli as a Gene-Fusion Marker"; Proc. Natl. Acad. Sci.; Vol. 83; (1986); pp. 8447-8451	
	A10	AYALA et al.; "Bacterial Single-Chain Antibody Fragments, Specific for Carcinoembryonic Antigen"; BioTechniques; Vol. 13, No. 5; (1992); pp. 790-799	
	A11	GOSHORN et al.; "Genetic Construction, Expression, and Characterization of a Single Chain Anti-Carcinoma Antibody Fused to B-Lactamase"; Cancer Res.; Vol. 53; (1993); pp. 2123-2127	
	A12	AMANN et al.; "Tightly Regulated tac Promoter Vectors Useful for the Expression of Unfused and Fused Proteins in Escherichia Coli"; Gene; Vol. 69; (1983); pp. 301-315	
	A13	BASHAWE; "Towards Generating Cytotoxic Agents at Cancer Sites"; Br. J. Cancer; Vol. 60; (1989); pp. 275-281	
	A14	PLUCKTHUN et al.; "Expression of Functional Antibody Fv and Fb Fragments in Escherichia Coli"; Methods in Enzymology; Vol. 178; (1989); pp. 497-515	
	A15	RODRIGUES et al.; "Development of a Humanized Disulfide-stabilized Anti-p 185 Fv-B-lactamase Fusion Protein for Activation of a Cephalosporin Doxorubicin Prodrug"; Cancer Research; January 1, 1995, Vol. 55; pp. 63-70, Baltimore, Maryland	

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	A16	GILLIES et al; Human Antibodies Hybridomas; Vol. 1, No. 1; pp. 47-54	
	A17	AXELSSON; Acta Chemica Scandanavica Series B; Vol. 39, No. 1; pp. 69-77	
	A18	PAULUS et al.; Behring Inst. Mitt.; No. 78; pp. 118-132	
	A19	BURGESS et al.; Journal of Cell Biology; Vol. 111; pp. 2129-2138	
	A20	LASAR et al; Molecular and Cellular Biology; Vol. 8, No. 3; pp. 1247-1252	
	A21	SCHWARTZ et al.; Proc. Natl. Acad. Sci. USA; Vol. 84; pp. 6408-6411	
	A22	LIN et al.; Biochemistry USA; Vol. 14; pp. 1559-1563	
	A23	HAISMA et al., "A monoclonal antibody- B-glucuronidase conjugate as a activator of the prodrug epirubicin-glucuronide for specific treatment of cancer", Br. J. Cancer, pp. 474-478, September 1992, Vol. 66, No. 3	
	A24	HE et al., "Functional expression of a single-chain anti-progesterone antibody fragment in the cytoplasm of a mutant Escherichia coli", Nucleic Acids Research, pp. 4009-4010, 1995, Vo. 23, No. 19, Oxford University Press	
	A25	QUI, J., Swartz, J., Georgiou, G., (1998), "Expression of Active Human Tissue-Type Plasminogen Activator in Escherichia coli", Applied and Environmental Microbiology, Dec. 1998, 64:4891-4896, American Society for Microbiology, Washington, D.C., USA	

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	A26	Wörn, A., and Plückthun, A., "An intrinsically stable antibody scFv fragment can tolerate the loss of both disulfide bonds and fold correctly", FEBS Letters 427 (1998) 357-361, Federation of European Biochemical Societies, Amsterdam, Holland	
	A27	Wörn, A., Auf der Maur, A., Escher, D., Honegger, A., Barberis, A., and Plückthun, A., "Correlation between in Vitro Stability and in Vivo Performance of Anti-CGN4 Intrabodies as Cytoplasmic Inhibitors", (2000) The Journal of Biological Chemistry Vol. 275, No. 4, Issue of January 28, 2795-2803, American Society for Biochemistry and Molecular Biology, Baltimore, Maryland, USA	
	A28	PROBA et al., "Functional antibody single-chain fragments from the cytoplasm of Escherichia coli: influence of thioredoxin reductase", Gene, Vol. 159, No. 2, pp. 203-207	
	A29	EMERY et al., "Strategies for Humanizing Antibodies" in Antibody Engineering, 2nd edition, Carol Borrebaeck, Ed., Oxford University Press, pp. 159-183	
	A30	BUCHNER et al., "A method for increasing the yield of properly folded recombinant fusion proteins", Anal Biochem, Vol. 205, pp. 263-270	
	A31	HOCHMAN et al., Biochemistry, 1976, Vol. 15, pp. 2706-2710	
	A32	GOTO et al., Journal of Molecular Biology, 1982, Vol. 156, pp. 911-926	
	A33	SKERRA et al., 1988, Vol. 240, 1038-1043	

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